Overview

Useful For

When a more targeted gene panel test was initially performed in our laboratory, this test allows for comprehensive reanalysis of a larger set of genes/gene regions

Evaluation of hematologic neoplasms, specifically of myeloid origin (eg, acute myeloid leukemia, myelodysplastic syndrome, myeloproliferative neoplasm, myelodysplastic/myeloproliferative neoplasm) at the time of diagnosis or possibly disease relapse, to help determine diagnostic classification and provide prognostic or therapeutic information for clinical management

Genetics Test Information

This test includes next-generation sequencing to evaluate for the following 42 genes and select intronic regions: *ANKRD26*, *ASXL1, BCOR, CALR, CBL, CEBPA, CSF3R, DDX41, DNMT3A,ELANE, ETNK1, ETV6, EZH2, FLT3, GATA1, GATA2, IDH1, IDH2, JAK2, KDM6A, KIT, KRAS, MPL, NPM1, NRAS, PHF6, PTPN11, RAD21, RUNX1, SETBP1, SH2B3, SF3B1, SRP72, SMC3, SRSF2, STAG2,TERT, TET2, TP53, U2AF1, WT1,* and *ZRSR2.*

Testing Algorithm

Only orderable as a reflex. Reflex testing is available upon request within 6 months of original NGAMT / Next-Generation Sequencing Acute Myeloid Leukemia, Therapeutic Gene Mutation Panel (*FLT3*, *IDH1*, *IDH2*, *TP53*) or NGAML / Next-Generation Sequencing, Acute Myeloid Leukemia, 11-Gene Panel sample submission.

This is a bioinformatics and variant review only for the added gene regions.

See Targeted Genes Interrogated by OncoHeme Next-Generation Sequencing in Special Instructions for a list of the genes and exons targeted by this test. Call 800-533-1710 for assistance with ordering.

Special Instructions

- Hematopathology Patient Information
- Targeted Genes Interrogated by OncoHeme Next-Generation Sequencing

Method Name

Only orderable as a reflex. For more information see NGAMT / Next-Generation Sequencing Acute Myeloid Leukemia, Therapeutic Gene Mutation Panel (*FLT3*, *IDH1*, *IDH2*, *TP53*) or NGAML / Next-Generation Sequencing, Acute Myeloid Leukemia, 11-Gene Panel.

Somatic Mutation Detection by Next-Generation Sequencing (NGS)

NY State Available

Yes

Specimen

Specimen Type

Varies

Specimen Required

Only orderable as a reflex. Reflex testing is available upon request within 6 months of original NGAMT / Next-Generation Sequencing Acute Myeloid Leukemia, Therapeutic Gene Mutation Panel (*FLT3*, *IDH1*, *IDH2*, *TP53*) or

NGAML / Next-Generation Sequencing, Acute Myeloid Leukemia, 11-Gene Panel sample submission.

No additional specimen is required. This is a bioinformatics review of additional gene regions not analyzed in the previously ordered NGAMT / Next-Generation Sequencing Acute Myeloid Leukemia, Therapeutic Gene Mutation Panel (*FLT3*, *IDH1*, *IDH2*, *TP53*) or NGAML / Next-Generation Sequencing, Acute Myeloid Leukemia, 11-Gene Panel. Call 800-533-1710 for assistance with ordering.

Forms

Hematopathology Patient Information (T676) in Special Instructions

Specimen Stability Information

Specimen Type	Temperature	Time
Varies	Varies	14 days

Clinical and Interpretive

Clinical Information

Next-generation sequencing (NGS) is a comprehensive molecular diagnostic methodology that can interrogate multiple regions of genomic tumor DNA in a single assay. Many hematologic neoplasms are characterized by morphologic or phenotypic similarities, but can have characteristic somatic mutations in many genes. In addition, many myeloid neoplasms lack a clonal cytogenetic finding at diagnosis (normal karyotype) but can be diagnosed and classified according to the gene mutation profile. The presence and pattern of gene mutations can provide critical diagnostic, prognostic, and sometimes therapeutic information for the managing physicians.

Reference Values

Only orderable as a reflex. For more information see NGAMT / Next-Generation Sequencing Acute Myeloid Leukemia, Therapeutic Gene Mutation Panel (*FLT3*, *IDH1*, *IDH2*, *TP53*) or NGAML / Next-Generation Sequencing, Acute Myeloid Leukemia, 11-Gene Panel.

An interpretive report will be provided.

Interpretation

Only orderable as a reflex within 6 months of initial testing. For more information see NGAMT / Next-Generation Sequencing Acute Myeloid Leukemia, Therapeutic Gene Mutation Panel (*FLT3*, *IDH1*, *IDH2*, *TP53*) or NGAML / Next-Generation Sequencing, Acute Myeloid Leukemia, 11-Gene Panel.

Mutations (gene alterations) identified, if present, using reference genome build GRCh37 (hg19). An interpretive report will be provided.

If this test is ordered in the setting of erythrocytosis and suspicion of polycythemia vera, interpretation requires correlation with a concurrent or recent prior bone marrow evaluation.

Cautions

This test is a targeted next-generation sequencing (NGS) (panel) assay that encompasses 42 genes with variable full exon, partial region (including select intronic or non-coding regions), or hot spot coverage (depending on specific locus). Therefore, this test will not detect other genetic abnormalities in genes or regions outside the specified target areas. The test detects single base substitutions (ie, point mutations), as well as small insertion or deletion type events, but it does not detect gene rearrangements (ie, translocations), gene fusions, copy number alterations, or

large scale (segmental chromosome region) deletions and complex changes.

This assay does not distinguish between somatic and germline alterations in analyzed gene regions, particularly with variant allele frequencies (VAF) near 50% or 100%. If nucleotide alterations in genes associated with germline mutation syndromes are present and there is also a strong clinical suspicion or family history of malignant disease predisposition, additional genetic testing and appropriate counseling may be indicated. Mutation cells detected between 5% and 10% VAF may indicate low-level (ie, subclonal) tumor populations, although the clinical significance of these findings may not be clear. A low incidence of gene mutations associated with myeloid neoplasms can be detected in nonmalignant hematopoietic cells in individuals with advancing age (clonal hematopoiesis of indeterminate potential, CHIP) and these may not be clearly distinguishable from tumor-associated mutations. Some apparent mutations classified as variants of undetermined significance (VUS) may represent rare or low frequency polymorphisms.

Prior treatment for hematologic malignancy could affect the results obtained in this assay. In particular, prior allogeneic hematopoietic stem cell transplant (HSCT) may cause difficulties in resolving somatic or polymorphic alterations, or in assigning variant calls correctly to donor and recipient fractions, if pertinent clinical or laboratory information (eg, chimerism engraftment status) is not provided.

Correlation with clinical, histopathologic and additional laboratory findings is required for final interpretation of these results. The final interpretation of results for clinical management of the patient is the responsibility of the managing physician.

Clinical Reference

1. Patel JP, Levine RL: How do novel molecular genetic markers influence treatment decisions in acute myeloid leukemia? Hematology Am Soc Hematol Educ Program 2012;2012:28-34

2. Lindsley RC, Ebert BL: The biology and clinical impact of genetic lesions in myeloid malignancies. Blood 2013;23:3741-3748

3. Patel JP, Gonen M, Figueroa ME, et al: Prognostic relevance of integrated genetic profiling in acute myeloid leukemia. N Engl J Med 2012;366:1079-1089

4. Haferlach T, Nagata Y, Grossman V, et al: Landscape of genetic lesions in 944 patients with myelodysplastic syndromes. Leukemia 2014;28:241-247

5. Vainchenker W, Delhommeau F, Constantinescu SN, Bernard OA: New mutations and pathogenesis of myeloproliferative neoplasms. Blood 2011;118:1723-1735

Performance

Method Description

This analysis requires that a previous smaller next-generation sequencing panel be performed at Mayo Clinic within the last 6 months (NGAMT / Next-Generation Sequencing Acute Myeloid Leukemia, Therapeutic Gene Mutation Panel [*FLT3*, *IDH1*, *IDH2*, *TP53*] or NGAML / Next-Generation Sequencing, Acute Myeloid Leukemia, 11-Gene Panel). An extended bioinformatics analysis is performed on the original data by the Mayo Clinic Clinical Genome Sequencing Laboratory bioinformatics pipeline and a variant call file is generated for final analysis and reporting of any additional pathogenic variants within genomic target regions present in the larger NGSHM / OncoHeme Next-Generation Sequencing for Myeloid Neoplasms.(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday, Wednesday, Friday

Analytic Time

14 days

Maximum Laboratory Time

21 days

Specimen Retention Time

DNA 3 months

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

81450

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
NGSFX	Reflex Analysis, NGSHM	In Process

Result ID	Test Result Name	Result LOINC Value
MP043	Specimen Type	31208-2
NFXID	Diagnosis/Indication	29308-4
601695	NGSFX Result	No LOINC Needed
601687	Pathogenic Mutations Detected	82939-0
601686	Interpretation	69047-9
601688	Clinical Trials	82786-5
601689	Variants of Unknown Significance	47997-2
601690	Additional Notes	48767-8
601691	Method Summary	49549-9
601692	Disclaimer	62364-5

Result ID	Test Result Name	Result LOINC Value
601693	NGSFX Panel Gene List	36908-2
601694	Reviewed By:	18771-6